

arabino nucleotides, 2'-O-CH₃ arabino nucleotides and 2'-dehydro-2'-CH₃ arabino nucleotides. A more preferred group include 2'-F arabino nucleotides, 2'-OH arabino nucleotides and 2'-O-CH₃, arabino nucleotides. A further preferred group include 2'-F arabino nucleotides and 2'-OH arabino nucleotides. Particularly preferred are 2'-F arabino nucleotides.

[0032] Particularly preferred oligonucleotides of the invention include selecting the nucleotides of the first portion of nucleotides to be 2'-SCH₃ ribonucleotides, 2'-NH₂ ribonucleotides, 2'-NH(C₁-C₂ alkyl) ribonucleotides, 2'-N(C₁-C₂ alkyl)₂ ribonucleotides, 2'-CH₃ ribonucleotides, 2'-CH=CH₂ ribonucleotides or 2'-C≡CH ribonucleotides and selecting the nucleotides of the further portion of nucleotides to be 2'-F ribonucleotides, 2'-O-(C₁-C₆ alkyl) ribonucleotides or 2'-O-(C₁-C₆ substituted alkyl) ribonucleotides wherein the substitution is C₁-C₆ ether, C₁-C₆ thioether, amino, amino(C₁-C₆ alkyl) or amino(C₁-C₆ alkyl)₂.

[0033] Further preferred oligonucleotides of the invention include selecting the nucleotides of said first portion of nucleotides to be 2'-CN arabino nucleotides, 2'-F arabino nucleotides, 2'-Cl arabino nucleotides, 2'-Br arabino nucleotides, 2'-N₃ arabino nucleotides, 2'-OH arabino nucleotides, 2'-O-CH₃ arabino nucleotides or 2'-dehydro-2'-CH₃ arabino nucleotides and selecting the nucleotides of the further portion of nucleotides to be 2'-F ribonucleotides, 2'-O-(C₁-C₆ alkyl) ribonucleotides or 2'-O-(C₁-C₆ substituted alkyl) ribonucleotides wherein the substitution is C₁-C₆ ether, C₁-C₆ thioether, amino, amino(C₁-C₆ alkyl) or amino(C₁-C₆ alkyl)₂.

[0034] Particularly preferred are oligonucleotide of the invention where each nucleotide of the first portion of nucleotides is a 2'-F arabino nucleotides or a 2'-OH arabino nucleotides and each nucleotide of the further portion of nucleotides is a 2'-O-(C₁-C₆ substituted alkyl) ribonucleotide

wherein the substitution is C₁-C₆ ether, C₁-C₆ thioether, amino, amino(C₁-C₆ alkyl) or amino(C₁-C₆ alkyl)₂.

[0035] In further preferred oligonucleotides of the invention the further portion of the plurality of nucleotides comprise at least two nucleotides joined together in a contiguous sequence that is position at the 3' terminus end of the oligonucleotide. In an additional preferred oligonucleotide of the invention the further portion of said plurality of nucleotides comprise at least two nucleotides joined together in a contiguous sequence that is position at the 5' terminus end of the oligonucleotide. In even further preferred oligonucleotides of the invention the further portion of the plurality of nucleotides comprise at least two nucleotides joined together in a contiguous sequence that is position at the 3' terminus end of the oligonucleotide and at least two nucleotides joined together in a contiguous sequence that is position at the 5' terminus end of the oligonucleotide. Preferred linkages for joining these nucleotides together in an oligonucleotide of the invention include 2'-5' phosphodiester linkages, 3'-methyleneephosphonate linkages, Sp phosphorothioate linkages, methylene(methylimino)linkages, dimethylhydrazino linkages, 3'-deoxy-3'-amino phosphoroamide linkages, amide 3 linkages or amide 4 linkages. Particularly preferred joining linkages are 2'-5' phosphodiester linkages, 3'-methyleneephosphonate linkages, Sp phosphorothioate linkages or methylene(methylimino) linkages.

[0036] In further preferred oligonucleotides of the invention, nucleotides for use in the further portion of nucleotides comprises 2'-alkylamino substituted nucleotides located at the 3' terminus, the 5' terminus or both the 3' and 5' terminus of the oligonucleotide. Particularly preferred are 2'-O-alkylamines such as 2'-O-ethylamine and 2'-O-propylamine.

[0037] Further oligonucleotides of the invention comprise oligonucleotides made up of a plurality of linked nucleotides at least two of which comprise nucleotides that are not 2'-deoxy-erythro-pentofuranosyl nucleotides and that have a C2' endo type pucker or an O4' endo type pucker and that are joined together in a contiguous sequence and other nucleotides comprising nucleotides that have a C3' endo type pucker. Preferred are oligonucleotides having the C3' endo type pucker nucleotides joined together in a contiguous sequence that is positioned 3' to the contiguous sequence of the nucleotides having the C2' endo type pucker or O4' endo type pucker. Further preferred oligonucleotides are oligonucleotides wherein the nucleotides having the C3' endo type pucker are joined together in a contiguous sequence that is positioned 5' to the contiguous sequence of having the C2' endo type pucker or O4' endo type pucker. Additional preferred oligonucleotide are oligonucleotides where a portion of the nucleotides having the C3' endo type pucker are joined together in a contiguous sequence that is positioned 3' to the contiguous sequence of nucleotides having the C2' endo type pucker or O4' endo type pucker and a further portion of nucleotides having the C3' endo type pucker are joined together in a contiguous sequence that is positioned 5' to the contiguous sequence of nucleotides having the C2' endo type pucker or O4' endo type pucker.

BRIEF DESCRIPTION OF THE DRAWINGS

[0038] Figure 1 illustrates a preferred group of nucleotide fragments for use in the B-form portion (the C2' endo / O4' endo portion) of oligonucleotides of the invention.

[0039] Figure 2 illustrates a preferred group of nucleotide fragments for use in the A-form portion (the C3' endo portion) of oligonucleotides of the invention.